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DATE: Monday, February 28, 2005

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☐	L5	poly(lactic acid-co-lysine) and RGD	23
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☐	L3	RGD with copolymer	46
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☐	L1	5700906.pn.	1

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☐ 1. Document ID: US 20030118692 A1

L5: Entry 1 of 23 File: PGPB Jun 26, 2003

DOCUMENT-IDENTIFIER: US 20030118692 A1
TITLE: Biodegradable polymer

Detail Description Paragraph:
[0113] To further control or regulate polymer interaction with cells, biomolecules, small molecules, or bioactive agents may be coupled to the hydroxyl groups or integrated into the polymer backbone (Barrera, D., et al., Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly(lactic acid-co-lysine). J. Am. Chem. Soc. 115: 11010-11, 1993; West, J. L., et al., Polymeric Biomaterials with Degradation Sites for Proteases Involved in Cell Migration. Macromolecules 32: 241-244, 1999; Mann, B. K., Smooth Muscle Cell Growth in Photopolymerized Hydrogels with Cell Adhesive and Proteolytically Degradable Domains: Synthetic ECM Analogs for Tissue Engineering. Biomaterials 22, 3045-3051; 2001). Alternatively, biomolecules, small molecules, or bioactive agents may be encapsulated within the bio-rubber and perhaps linked to it using non-covalent interactions. Attachment of the moiety to the bio-rubber results in a slower release rate because it is released from the material as it degrades. In contrast, if the moiety is encapsulated within the bio-rubber, it may diffuse out of the material before the polymer degrades.

Detail Description Paragraph:
[0114] For example, biomolecules such as growth factors may be exploited to recruit cells to a wound site or promote specific metabolic or proliferative behavior in cells that are at the site or seeded within the matrix. Exemplary growth factors include, without limitation, TGF-.beta., acidic fibroblast growth factor, basic fibroblast growth factor, epidermal growth factor, IGF-I and II, vascular endothelial-derived growth factor, bone morphogenetic proteins, platelet-derived growth factor, heparin-binding growth factor, hematopoetic growth factor, and peptide growth factor. Integrins and cell adhesion sequences (e.g., the RGD sequence) may be attached to the bio-rubber to facilitate cell adhesion. Integrins are part of a large family of cell adhesion receptors that are involved in cell-extracellular matrix and cell-cell interactions. The RGD sequence, present in proteins such as fibronectin, has been shown to be active in promoting cell adhesion and proliferation (Massia, et al., J. Cell. Biol. 114:1089, 1991). Extracellular matrix components, e.g., collagen, fibronectin, laminin, elastin, etc., may be combined with bio-rubber to manipulate cell recruitment, migration, and metabolism and the degradation and mechanical properties of the material. Proteoglycans and glycosaminoglycans may also be covalently or non-covalently attached to bio-rubber.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 6855329 B1

L5: Entry 2 of 23 File: USPT Feb 15, 2005

DOCUMENT-IDENTIFIER: US 6855329 B1
TITLE: Surface coating spatially controlled patterns

Brief Summary Text (29):
Copolymers with amino acids may be synthesised, for example glycolic acid and glycine, or lactic acid and lysine (Barrera et al (1993) J. Am Chem Soc 115, 11010-11011 and Cook et al (1997) J Biomed Mat Res 35, 513-523). These may be useful for immobilizing other molecules, for example via the lysyl .epsilon.-amino moieties. These polymers may be used to attach peptides to surfaces using covalent bonds. For example, peptides may be attached to poly (lactic acid-co-lysine) using 1,1'-carbonyl-diimidazole (CDI, Aldrich) as a linking agent as described in the above references.

Brief Summary Text (49):
Examples of ligands that may be used include adhesion proteins, for example fibronectin and vitronectin, or fragments thereof, that are recognized by cytoskeletally associated receptors in the cell membrane, known as integrins. The receptors bind into a small domain on the adhesion proteins, for example the peptide sequence RGD, which is found in many adhesion proteins, and binds to many integrins. Varying the sequence or flanking sequences can alter the binding affinity of a receptor for the peptide or protein containing it. The density of the ligand may affect the cellular response, and it will be appreciated that it may be necessary to control the density of the ligand, for example RGD peptide, to get the optimum density for cell spreading.

Brief Summary Text (77):
Two important examples of tissue engineering applications in which the method may be used are directed nerve regeneration and new blood vessel formation (vasculogenesis). For nerve regeneration applications, patterns composed of the peptide sequence IKVAV (SEQ ID NO:2) may be used to force or at least encourage nerve cell growth to follow predetermined pathways, i.e. between two severed points of a nerve or towards a denerved tissue. Experimental results have proved that nerve cells adhere and grow along lines generated by the method of the invention (FIGS. 1,2 and 6 and Example 1). For vasculogenesis applications, endothelial cells can be forced to grow along patterns composed of the peptide sequence RGD. Experimental results of directed endothelial cell growth are shown in FIG. 3.

Brief Summary Text (116):
For example, if a biotin/avidin/biotin anchor/adapter/tag system is used, the surface is washed and exposed to biotinylated ligand (for example, RGD or IKVAV (SEQ ID NO:2)). This ligand couples with the avidin to form a pattern of the ligand on the surface. A full protocol is given in Example 1.

Brief Summary Text (126):
Multiple patterning can be achieved by more than one addition of adapter. After each addition a tagged ligand is immobilized. In general, useful combinations may include cell adhesive ligands that are specific for unique cell types. For example, galactose-terminated polyethylene glycol chains bind hepatocytes whilst RGD-containing sequences bind virtually all cell types. Therefore, hepatocytes can patterned onto surfaces and then surrounded by endothelial cells. This can encourage cell-to-cell contacts that are thought to be vital in ensuring that hepatocytes function successfully.

Brief Summary Text (132):
The articles and methods of the invention may also be used to accelerate wound healing. Patterned templates may encourage keratinocytes to migrate into wound areas by stimulating integrin mediated cell migration along lines of RGD peptide. Again, growth factors may be released from the templates to stimulate wound healing.

Brief Summary Paragraph Table (1):
TABLE 1 Cell binding domain sequences of extracellular matrix proteins Protein Sequence Role Fibronectin RGDS (SEQ ID NO:5) Adhesion of most cells, via .alpha..beta. receptor LDV Adhesion

REDV (SEQ ID NO:4) Adhesion Vitronectin RGDV (SEQ ID NO:6) Adhesion of most cells, via .alpha..beta. receptor Laminin A LRGDN (SEQ ID NO:7) Adhesion IKVAV (SEQ ID NO:2) Neurite extension Laminin B1 YIGSR (SEQ ID NO:1) Adhesion of many cells, via 67kDA laminin receptor PDSGR (SEQ ID NO:8) Adhesion Laminin B2 RNIAEIIK DA (SEQ ID Neurite extension NO:9) Collagen I RGDT (SEQ ID NO:10) Adhesion of most cells DGEA (SEQ ID NO:11) Adhesion of platelets, other cells Thrombo- RGD Adhesion of most cells spondin VTXG (SEQ ID NO:12) Adhesion of platelets After [5]

Drawing Description Text (12):
FIG. 11: Spatially controlled adhesion and spreading of biovine aortic endothelial cells on 70 and 50 .mu.m-wide lines containing RGD peptides. Panels A, B, D are transmission images. Panel C is a phase contrast image.

Detailed Description Text (52):
Images are shown in FIGS. 11 and 12. The BAECs adhered and spread on the RGD-functionalised (biotin-G.sub.11 GRGDS (SEQ ID NO:18)) lines but did not adhere to unfunctionalised areas between the lines. Complete cell coverage of the 70 and 50 .mu.m width lines was achieved, but little cell adhesion occurred to the 30 or 12 .mu.m-wide lines.

Other Reference Publication (1):
Barrera, et al., "Synthesis and RGD peptide modification of a new biodegradable copolymer. Poly (lactic acid co-lysine)," J Am Chem Soc 115:11010-11011 (1993).

Other Reference Publication (2):
Cook, et al., "Characterization and development of RGD-peptide-modified poly(actic acid-co-lysine) as an interactive, resorbable biomaterial," Journal of Biological Materials Research 35:513-523 (1997).

☐ 3. Document ID: US 6800481 B1

L5: Entry 3 of 23 File: USPT Oct 5, 2004

DOCUMENT-IDENTIFIER: US 6800481 B1
TITLE: Stable macroscopic membranes formed by self-assembly of amphiphilic peptides and uses therefor

Detailed Description Text (59):
Certain peptide polymers of this class contain sequences which are similar to the cell attachment ligand RGD. The suitability of these biomaterials for supporting in vitro cell growth was tested by introducing a variety of cultured primary and transformed cells to homopolymer sheets of EAK16, RAD16, RADA16, and heteropolymers of RAD16 and EAK16. The RAD-based peptides are of particular interest because the similarity of this sequence to RGD. The RAD sequence is a high affinity ligand present in the extracellular matrix protein tenascin and is recognized by integrin receptors.

Detailed Description Text (169):
Nerve growth factor differentiated PC12 cells have been used extensively in studies of neurite outgrowth. PC12 cells upregulate the number of calcium-dependent and -independent cell adhesion receptors in response to nerve growth factor. Cell attachment and neurite outgrowth from nerve growth factor differentiated PC12 cells was examined on membranes of RAD16 and EAK16 in order to determine whether membranes containing RGD-like sequences would preferentially support these cell activities. Neurite outgrowth on peptide membranes is of interest for potential applications of nerve repair.

Other Reference Publication (32):
Barrera, D. et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolyner: Poly(lactic acid-co-lysine)", J. Am. Chem. Soc. 115:11010-11011 (1993).

Other Reference Publication (34):
Lin, H.B. et al., "Synthesis, surface, and cell-adhesion properties of polyurethanes containing covalently grafted RGD-peptides", J. of Biomedical Materials Research 28:329-342 (1994).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 4. Document ID: US 6740310 B2

L5: Entry 4 of 23 File: USPT May 25, 2004

DOCUMENT-IDENTIFIER: US 6740310 B2
TITLE: Porous particles comprising excipients for deep lung delivery

Other Reference Publication (40):
Barrera, D.A., et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly(lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010-11011 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 6652837 B1

L5: Entry 5 of 23 File: USPT Nov 25, 2003

DOCUMENT-IDENTIFIER: US 6652837 B1
TITLE: Preparation of novel particles for inhalation

Detailed Description Text (57):
Targeting molecules can be attached to the particles via reactive functional groups on the particles. For example, targeting molecules can be attached to the amino acid groups of functionalized polyester graft copolymer particles, such as poly(lactic acid-co-lysine) (PLAL-Lys) particles. Targeting molecules permit binding interaction of the particle with specific receptor sites, such as those within the lungs. The particles can be targeted by attachment of ligands which specifically or non-specifically bind to particular targets. Exemplary targeting molecules include antibodies and fragments thereof including the variable regions, lectins, and hormones or other organic molecules capable of-specific binding, for example, to receptors on the surfaces of the target cells.

Other Reference Publication (41):
Barrera, et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J Am. Chem. Soc., 115: 11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

6. Document ID: US 6635283 B2

L5: Entry 6 of 23 File: USPT Oct 21, 2003

DOCUMENT-IDENTIFIER: US 6635283 B2
** See image for Certificate of Correction **
TITLE: Aerodynamically light particles for pulmonary drug delivery

Other Reference Publication (42):
Barrera, et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J Am. Chem. Soc., 115: 11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

7. Document ID: US 6447753 B2

L5: Entry 7 of 23 File: USPT Sep 10, 2002

DOCUMENT-IDENTIFIER: US 6447753 B2
TITLE: Porous particles for deep lung delivery

Other Reference Publication (42):
Barrera, D.A., et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly(lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010-11011 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

8. Document ID: US 6447752 B2

L5: Entry 8 of 23 File: USPT Sep 10, 2002

DOCUMENT-IDENTIFIER: US 6447752 B2
TITLE: Amorphous porous particles for deep lung delivery

Other Reference Publication (42):
Barrera, D.A., et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly(lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010-11011 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

9. Document ID: US 6436443 B2

L5: Entry 9 of 23 File: USPT Aug 20, 2002

DOCUMENT-IDENTIFIER: US 6436443 B2
** See image for Certificate of Correction **
TITLE: Porous particles comprising excipients for deep lung delivery

Other Reference Publication (42):
Barrera, D.A., et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010-11011 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 10. Document ID: US 6399102 B1

L5: Entry 10 of 23 File: USPT Jun 4, 2002

DOCUMENT-IDENTIFIER: US 6399102 B1
** See image for Certificate of Correction **
TITLE: Aerodynamically light particles for pulmonary drug delivery

Other Reference Publication (41):
Barrera, et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J Am. Chem. Soc., 115: 11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 11. Document ID: US 6365173 B1

L5: Entry 11 of 23 File: USPT Apr 2, 2002

DOCUMENT-IDENTIFIER: US 6365173 B1
TITLE: Stereocomplex polymeric carriers for drug delivery

Other Reference Publication (2):
Barrera, et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," JACS 115:11010-11011 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 12. Document ID: US 6316581 B1

L5: Entry 12 of 23 File: USPT Nov 13, 2001

DOCUMENT-IDENTIFIER: US 6316581 B1
TITLE: Bioresorbable copolymers

Brief Summary Text (9):
The prior art discloses examples in which biopolymer chains are decorated to facilitate the attachment of various bioactive substances. Such decoration is recognized as being important in tissue engineering applications. Barrera et al., Macromolecules, 28, 425 (1995); Fietier et al., Polym. Bull. (Berlin) 24, 349 (1990). Barrera et al., Macromolecules, 28, 425 (1995), prepared a copolymer of poly(lactic acid-co-lysine) with RGD attached to the lysine residues at a surface concentration of 310 fmol/cm.sup.2. The RGD peptide functions to promote cell adhesion. However, the use of this copolymer has been restricted because the molecular weight of poly(lactic acid-co-lysine) copolymers decreased significantly relative to [L]-LA homopolymerization, even with low 3-[N-(carbonyl-benzoxy)-L-lysyl]-6-L-methyl-2,5-morpholinedione co-monomer feed ratios.

13. Document ID: US 6306821 B1

L5: Entry 13 of 23 File: USPT Oct 23, 2001

DOCUMENT-IDENTIFIER: US 6306821 B1
TITLE: Functionalized poly(propylene fumarate) and poly(propylene fumarate-co-ethylene glycol)

Detailed Description Text (12):
Peptides that can be coupled to the activated PEG-tethered PPF include but are not limited to: RGD, YIGSR, REDV, IKVAV, and KRSR peptides. Proteins that can coupled to the activated PEG-tethered PPF include but are not limited to members of the transforming growth factor beta superfamily, including the bone morphogenetic proteins, as well as basic fibroblast growth factor, platelet derived growth factor, and insulin like growth factor. Other examples include extracellular matrix molecules such as osteo-pontin, osteonectin, osteocalcin, and bone sialoprotein. Protein fragments that can coupled to the activated PEG-tethered PPF include but are not limited to any fragments of the above proteins comprising 3-30 amino acids. Hyaluronic acid is an example of a suitable proteoglycan. Carbohydrates that can coupled to the activated PEG-tethered PPF include but are not limited to: starch, cellulose, and chitin.

Detailed Description Text (24):
The particular peptide sequence plays a ubiquitous role on cell adhesion process. The peptide sequence arginine-glycine-aspartic acid (RGD) has been established as a minimal peptide sequence responsible for integrin/ligand interaction on many adhesive proteins such as fibronectin, vitronectin, collagen, and laminin. Therefore, synthetic RGD peptides have been immobilized into polymeric materials to improve specific cell attachment. Cook et al modified poly(lactic acid-co-lysine) with RGD peptide for possible application as a temporary scaffold for cell transplantation. Hem and Hubbell incorporated RGD-peptide sequences into PEG diacrylate networks by photopolymerization and reported that RGD peptide required a certain hydrophilic spacer for specific cell spreading into nonadhesive PEG diacrylate matrices.

CLAIMS:

2. The poly(propylene fumarate) according to claim 1 wherein the peptide is selected from the group consisting of RGD, YIGSR, REDV, IKVAV, and KRSR peptides.

7. The poly(propylene fumarate) network according to claim 6 wherein the peptide is selected from the group consisting of RGD, YIGSR, REDV, IKVAV, and KRSR peptides.

12. The poly(propylene fumarate-co-ethylene glycol) according to claim 11 wherein the peptide

is selected from the group consisting of RGD, YIGSR, REDV, IKVAV, and KRSR peptides.

17. The poly(propylene fumarate-co-ethylene glycol) network according to claim 16 wherein the peptide is selected from the group consisting of RGD, YIGSR, REDV, IKVAV, and KRSR peptides.

☐ 14. Document ID: US RE37053 E

L5: Entry 14 of 23 File: USPT Feb 13, 2001

DOCUMENT-IDENTIFIER: US RE37053 E
** See image for Certificate of Correction **
** See image for Reexamination Certificate **
TITLE: Particles incorporating surfactants for pulmonary drug delivery

Other Reference Publication (6):
Barrera et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010 (1993).

☐ 15. Document ID: US 6153596 A

L5: Entry 15 of 23 File: USPT Nov 28, 2000

DOCUMENT-IDENTIFIER: US 6153596 A
** See image for Certificate of Correction **
TITLE: Polycationic oligomers

Brief Summary Text (32):
Poly(lactic acid) is a biodegradable polymer widely used as a biomedical material. The random copolymer, poly(lactic acid-co-lysine), has been prepared and suggested as an alternative to poly(lactic acid) in biomedical applications, particularly as a matrix material for tissue engineering. See: D. A. Barrera et al. (1993) J. Am. Chem. Soc. 115:11010-11011 and D. A. Barrera et al. (1995) Macromolecules 28:425-432. Incorporation of lysine residues into poly (lactic acid) provides chemically reactive sites for derivatizing the material to alter its surface with biologically active moieties. The first copolymer prepared was reported to have an average molecular weight of 64,000 g/mol and to contain 1.3 mol % lysine. Copolymers ranging in molecular weight from about 7,000 to 95,000 and lysine mol % from 2.4 to 6.4 were also reported. Materials with properties desirable for biomedical applications are reported to contain 1-10 mol % lysine. Higher concentrations of lysine in the co-polymer are said to alter the physical characteristics of the polymer poly(lactic acid) and to be deleterious to degradability. It was also reported that the copolymer was derivatized via its lysine residues with a cell adhesion promoting peptide.

Other Reference Publication (7):

Barrera, D.A. et al. (1995), "Copolymerization and Degradation of Poly-(lactic acid-co-lysine)," Macromolecules 28:425-432.

Other Reference Publication (8):
Barrera, D.A. et al. (1993), "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly(lactic acid-co-lysine," J. Am. Chem. Soc. 115:11010-11011.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 16. Document ID: US 6136295 A

L5: Entry 16 of 23 File: USPT Oct 24, 2000

DOCUMENT-IDENTIFIER: US 6136295 A
**** See image for Reexamination Certificate ****
TITLE: Aerodynamically light particles for pulmonary drug delivery

Other Reference Publication (4):
Barrera, et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J Am. Chem. Soc., 115: 11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 17. Document ID: US 5985309 A

L5: Entry 17 of 23 File: USPT Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5985309 A
**** See image for Certificate of Correction ****
**** See image for Reexamination Certificate ****
TITLE: Preparation of particles for inhalation

Detailed Description Text (54):
Targeting molecules can be attached to the particles via reactive functional groups on the particles. For example, targeting molecules can be attached to the amino acid groups of functionalized polyester graft copolymer particles, such as poly(lactic acid-co-lysine) (PLAL-Lys) particles. Targeting molecules permit binding interaction of the particle with specific receptor sites, such as those within the lungs. The particles can be targeted by attachment of ligands which specifically or non-specifically bind to particular targets. Exemplary targeting molecules include antibodies and fragments thereof including the variable regions, lectins, and hormones or other organic molecules capable of specific binding, for example, to receptors on the surfaces of the target cells.

Other Reference Publication (31):
Barrera et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

18. Document ID: US 5955343 A

L5: Entry 18 of 23 File: USPT Sep 21, 1999

DOCUMENT-IDENTIFIER: US 5955343 A
TITLE: Stable macroscopic membranes formed by self-assembly of amphiphilic peptides and uses therefor

Detailed Description Text (59):
Certain peptide polymers of this class contain sequences which are similar to the cell attachment ligand RGD. The suitability of these biomaterials for supporting in vitro cell growth was tested by introducing a variety of cultured primary and transformed cells to homopolymer sheets of EAK16, RAD16, RADA16, and heteropolymers of RAD16 and EAK16. The RAD-based peptides are of particular interest because the similarity of this sequence to RGD. The RAD sequence is a high affinity ligand present in the extracellular matrix protein tenascin and is recognized by integrin receptors.

Detailed Description Text (170):
Nerve growth factor differentiated PC12 cells have been used extensively in studies of neurite outgrowth. PC12 cells upregulate the number of calcium-dependent and -independent cell adhesion receptors in response to nerve growth factor. Cell attachment and neurite outgrowth from nerve growth factor differentiated PC12 cells was examined on membranes of RAD16 and EAK16 in order to determine whether membranes containing RGD-like sequences would preferentially support these cell activities. Neurite outgrowth on peptide membranes is of interest for potential applications of nerve repair.

Other Reference Publication (32):
Barrera, Denise et al. "Synthesis and RGD Peptide Modification of a New Biodegradable Copolyner: Poly(lactic acid-co-lysine)," J. Am. Chem. Soc. 115:11010-11011 (1993).

Other Reference Publication (34):
Lin, Horng-Ban et al. "Synthesis, surface, and cell-adhesion properties of polyurethanes containing covalently grafted RGD-peptides," J. of Biomedical Materials Research 28:329-342 (1994).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw Desc | Image

19. Document ID: US 5916585 A

L5: Entry 19 of 23 File: USPT Jun 29, 1999

DOCUMENT-IDENTIFIER: US 5916585 A
TITLE: Materials and method for the immobilization of bioactive species onto biodegradable polymers

Brief Summary Text (18):
Bioactive species could be attached to a hydrophobic biodegradable polymer through chemically functional groups on the components of the polymer. However, many biodegradable polymers lack free chemically functional groups altogether or have such reduced numbers that significant quantities of bioactive species cannot be immobilized thereto. For example, the biodegradable

polymers poly(lactic acid) and poly(glycolic acid) do not contain any chemically functional groups along the hydrocarbon backbone of the materials to which a bioactive species can be covalently coupled. One strategy that has been proposed for introducing functional groups into poly(lactic acid) is the copolymerization of lactide with a cyclic monomer of lactic acid and the amino acid lysine to create poly(lactic acid-co-lysine) (see U.S. Pat. No. 5,399,665, issued to Barrera, et. al.). This copolymer provides side chains that terminate in amino (NH.sub.2) groups. These amino groups can be used as attachment sites for the immobilization of bioactive species. Since this method chemically alters the polymer, many of the properties of the polymer are subject to change. For example, the degradation rate and the tensile strength may be effected by the alteration to the polymer. The processing of the polymer may also be effected by altering the hydrocarbon backbone of the polymer.

Other Reference Publication (8):
Hirano, Y., et al. Cell-attachment activities of surface immobilized oligopeptides RGD, RGDS, RGDV, RGDT, and YIGSR toward five cell lines. J. Biomater. Sci. Polymer Edn. 1993;v4 n3:235-243.

Other Reference Publication (18):
Lin, H-B., Cooper, S.L. Polyurethane copolymers containing covalently attached RGD-Peptide: synthesis and cell adhesion studies. Mat. Res. Soc. Symp. Proc. 1992;252:185-192.

Other Reference Publication (28):
Cook, Alonzo D. The Evaluation of RGD-Peptide Modified Poly(lactic acid-co-lysine) as a Resorbable, Interactive Biomaterial. Massachusetts Institute Of Technology, Feb. 1996.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 20. Document ID: US 5874064 A

L5: Entry 20 of 23 File: USPT Feb 23, 1999

DOCUMENT-IDENTIFIER: US 5874064 A
**** See image for Certificate of Correction ****
**** See image for Reexamination Certificate ****
TITLE: Aerodynamically light particles for pulmonary drug delivery

Other Reference Publication (26):
Barrera et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010 (1993).

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 21. Document ID: US 5855913 A

L5: Entry 21 of 23 File: USPT Jan 5, 1999

DOCUMENT-IDENTIFIER: US 5855913 A
TITLE: Particles incorporating surfactants for pulmonary drug delivery

Other Reference Publication (4):
Barrera et al., "Synthesis and RGD Peptide Modification of a New Biodegradable Copolymer: Poly (lactic acid-co-lysine)," J. Am. Chem. Soc., 115:11010 (1993).

☐ 22. Document ID: US 5654381 A

L5: Entry 22 of 23 File: USPT Aug 5, 1997

DOCUMENT-IDENTIFIER: US 5654381 A
**** See image for Certificate of Correction ****
TITLE: Functionalized polyester graft copolymers

Brief Summary Text (36):
This illustrates the presence and availability of free amino acids containing carboxyl groups on the surface of the copolymer. The carboxylic groups can be utilized for the attachment of biologically active molecules, such as RGD peptides. In addition, in a neutral aqueous environment, the poly(aspartic acid) side chains will be deprotonated, offering a negatively charged environment, which can allow the ionic attachment of positively charged molecules.

Brief Summary Text (45):
For example, peptides possessing an RGD (arginine-glycine-aspartic acid) amino acid sequence may be attached to the graft copolymers. The RGD sequence, present in proteins such as fibronectin, has been shown to be active in promoting cell adhesion and growth. Massia, S. P. and Hubbell, J. A., J. Cell. Biol., 114:1089 (1991). Incorporation of RGD sequences as part of the copolymer structure thus can enhance cell growth. This can be useful in some cases for tissue engineering, wherein polyesters to which cells such as hepatocytes do not normally adhere can be modified to enable them to be used successfully as supports for cell growth. Additionally, biologically active molecules may be incorporated into the copolymer which promote the adhesion and growth of a particular cell type in vivo.

Other Reference Publication (10):
Massia, S.P. and Hubbell, "An RGD Spacing Of 440 nm Is Sufficient For Integrin .alpha.v.beta.3-Mediated Fibroblast Spreading And 140 nm for Focal Contact And Stress Fiber Formation", J.A., J. Cell. Biol., 114:10891100 (1991).

Other Reference Publication (13):
Barrera, et al., "Synthesis And RGD Peptide Modification Of A New Biodegradable Copolymer: Poly (lactic acid-co-lysine)", J. Am. Chem. Soc., 115:11010-11011 (1993).

☐ 23. Document ID: US 5399665 A

L5: Entry 23 of 23 File: USPT Mar 21, 1995

DOCUMENT-IDENTIFIER: US 5399665 A
TITLE: Biodegradable polymers for cell transplantation

Detailed Description Text (37):
It is important for optimal cellular function to be able to manipulate the surface chemistry of the polymer device. An important example of this is the attachment of an RGD peptide which has been shown to promote cell adhesion. The attachment of this adhesion moiety to the reactive side chains such as free amino groups on the polymer surface can be achieved by either of two methods.

Detailed Description Text (38):
The first method involves activating the C-terminus carboxylic acid of the peptide, and then reacting this group with the amino groups on the polymer surface. The C-terminus carboxylic acid can be activated by several methods as indicated in Table I. A preferred reagent is 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC) which produces an O-acyl-isourea. This activated species will react readily with free amino groups (Yamada, H.; Imoto, T.; Fujita, K.; Okazaki, K.; and Motomura, M.; "Selective Modification of Aspartic Acid-101 in Lysozyme by Carbodiimide Reaction," Biochemistry, 20, 4836-4842 (1981); Hoare, D. G. and Koshland, D. E. Jr., "A Method for the Quantitative Modification and Estimation of Carboxylic Acid Groups in Proteins," The Journal of Biological Chemistry, 242, 2447-2453 (1967); Sheehan, J. C.; Preston, J.; Cruickshank, P. A., "A Rapid Synthesis of Oligopeptide Derivatives without Isolation of Intermediates," Journal of the American Chemical Society, 87, 2492-2493 (1965)). However, biologically active moieties such as the RGDS peptide contain two carboxylic acid groups, one at the C-terminus and the other on the aspartic acid residue. If the C-terminus carboxylic acid is to be used to chemically attach the peptide to the polymer surface then the aspartic acid residue must be protected. A completely protected RGDS peptide can be synthesized by those skilled in the art. After attachment the peptide side chains of the peptide would have to be deprotected.

Detailed Description Text (65):
All the glassware was dried overnight in a 130.degree. C. oven and cooled under argon. To the reaction vessel was added 225 ml SiEt.sub.3 H (1.4M), 9.9 g of the copolymer from example 2, 225 ml methylene chloride, 1.8 g PdCl.sub.2 (0.010M), and 2.1 ml NEt3 (0.016M) in the order listed. The reaction was stirred at room temperature for five days. The catalyst, PdCl.sub.2, was removed by filtration. 150 ml of methanol was added and let stand 10 minutes, then the solution dumped into excess methanol, approximately 3000 ml. Let stand 30 minutes, and then the precipitate collected by vacuum filtration. The polymer was dried under vacuum. The product from this reaction is poly (lactic acid-co-lysine). The yield is 79% which is 7.8 g. The molecular weights are: Mn=31,500, Mw=44,100, Mz=69,700. Proton NMR indicates that 75% of the protecting residues were removed while amino acid analysis indicates that 88% of the lysine units remain in the polymer. The IR spectrum was consistent and DSC analysis shows two melting peaks with the onset of the more intense peak at Tm=159.2.degree. C. and Tg=55.7.degree. C.

Detailed Description Text (69):
Solvent Casting: Poly (lactic acid-co-lysine) from Example 3 (100 mg) was weighed out into a standard 10 ml glass beaker. Chloroform (2 ml) was added to dissolve the polymer. The chloroform was allowed to evaporate very slowly over a 48 hour period. In order to remove the film from the beaker it was submersed in water for 4 hours. The free standing film is easily handled without breaking and can be cut with a razor blade or scissors. Its appearance is translucent.

Detailed Description Text (70):
Compression Molding: Poly (lactic acid-co-lysine) from Example 3 is ground to a fine powder. The powder (150 mg) is put into a die (1.4 cm diameter) and compressed at 10,000 psi for 30 minutes while the top and bottom compression plates are at 100.degree. C. This type of film can be easily handled, but higher temperatures are necessary to obtain a translucent film. Higher temperatures also cause the film to become brittle.

Detailed Description Text (72):
The hydrolytic degradation of the poly (lactic acid-co-lysine).

Detailed Description Text (73):

This example illustrates the hydrolytic degradation of the poly (lactic acid-co-lysine) described in example 3.

Detailed Description Text (74):
The solvent cast films of poly (lactic acid-co-lysine) from Example 4 were immersed in PBS pH 7.2 at 37.degree. C. with rotational agitation at 120 rpm. The buffer was changed weekly and the films were sacrificed at various time points. These films degrade more quickly than homopolymers of lactic acid. By five weeks, the Mw of the copolymer was half of its original value and the films had lost integrity, breaking up into many pieces. The remaining weight of the films decreased gradually. By 23 weeks more than 40% of the weight was lost. Lactic acid was also released into the buffer, as determined by an enzymatic assay.

Other Reference Publication (42):
Barrera, D. et al., "Poly (lactic acid-co-Lysine); A new material for organ regeneration," AIChE Abstract (Nov. 18, 1991).

Other Reference Publication (65):
Hirano, Y., Hayashi, T., Goto, K., and Nakajima, A., "Synehesis and Evaluation of Oligopeptide RGDS Exhibiting Cell-Attachment Activity," Polymer Bulletin, vol. 26, pp. 363-370 (1991).

Other Reference Publication (69):
Lin, H., et al., "Synthesis of a Novel Polyurethane Copolymer Containing Covalently Attached RGD Peptide," Journal of Biomaterials Science, Polymer edition, (1991).

Other Reference Publication (73):
Massia, S., and Hubbell, J., "RGD Spacing of 440 nm is Sufficient for Integrin alpha-beta-3-Mediated Fibroblast Spreading and 140 nm For Focal Contact and Stress Fiber Formation," J. Cell Biology (1991).

Other Reference Publication (79):
Olivieri, M., et al., "Surface Characterization of ArginylGlycylAspartic Acid (RGD) Peptide Films," The 17th Annual Meeting of the Society for Biomaterials, pp. 131 (1991).

CLAIMS:

5. The polymer of claim 4 wherein the biologically active moieties are selected from the group consisting of GRGDY, YIGSR and other RGD peptides.

10. The process of claim 9 wherein the biologically active moleties are selected from the group consisting of GRGDY, YIGSR and other RGD peptides.

17. The process of claim 13 wherein the biologically active moieties are selected from the group consisting of GRGDY, YIGSR and other RGD peptides.

Term	Documents
POLY	338299
POLIES	67
POLYS	758

LACTIC	74739
LACTICS	41
ACID-CO-LYSINE	61
ACID-CO-LYSINES	0
RGD	9038
RGDS	1486
((POLY ADJ (LACTIC ADJ ACID-CO-LYSINE)) AND RGD).PGPB,USPT,USOC.	23
(POLY(LACTIC ACID-CO-LYSINE) AND RGD).PGPB,USPT,USOC.	23

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WEST Search History

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DATE: Monday, February 28, 2005

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L8	poly(Lys-Asp) or poly(k$1D)	2
☐	L7	poly(Lys-Asp)	1
☐	L6	poly(Lys-Asp) and $2polymer?	1
☐	L5	19990402	0
☐	L4	19990402	0
☐	L3	19990402	0
☐	L2	20040209818	1
☐	L1	0209818	2

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 20040022726 A1

L8: Entry 1 of 2 File: PGPB Feb 5, 2004

DOCUMENT-IDENTIFIER: US 20040022726 A1
TITLE: Methods and compositions for intravesical therapy of bladder cancer

Summary of Invention Paragraph:
[0051] Any aspect of the present can be wherein the carrier molecule is a polymer of the structure [HSG].sub.m-polymer backbone-[DOTA-therapeutic agent].sub.n wherein HSG comprises a recognition hapten wherein m.gtoreq.1 and n.gtoreq.1. (M can be 1 or 2, and n can from 1 to about 100.) The method of claim 1, wherein the carrier molecule can be a biocompatible polymer. The carrier molecule can be a polyamino acid or polypeptide, wherein the amino acids are D-, L-, or both. The carrier molecule can be a polyamino acid or polypeptide selected from the group consisting of polylysine, polyglutamic acid, polyaspartic acid, a poly(Lys-Glu) co-polymer, a poly(Lys-Asp) copolymer, a poly(Lys-Ala-Glu-Tyr) (KAEY; 5:6:2:1) co-polymer or a polypeptides of from 2-50 residues chain length. The carrier molecule can be selected from the group consisting of poly(ethylene) glycol (PEG), N-(2-hydroxypropyl)methacrylamide (HMPA) copolymers, poly(styrene-co-maleic acid/anhydride (SMA), poly(divinylether maleic anhydride) (DIVEMA), polyethyleneimine, ethoxylated polyethyleneimine, dendrimers, poly(N-vinylpyrrolidone) (PVP) epsilon-[histaminyl-succinyl-g- lycyl]-lysine amide, and apo-metallothionein coupled to p-bromoacetamido-benzyl-DTPA. The carrier molecule can be an immunogenic agent to which secondary recognition antibodies can be raised.

CLAIMS:

18. The method of claim 17, wherein the carrier molecule is a polyamino acid or polypeptide selected from the group consisting of polylysine, polyglutamic acid, polyaspartic acid, a poly (Lys-Glu) co-polymer, a poly(Lys-Asp) copolymer, a poly(Lys-Ala-Glu-Tyr) (KAEY; 5:6:2:1) co-polymer or a polypeptides of from 2-50 residues chain length.

51. The method of claim 50, wherein the carrier molecule is a polyamino acid or polypeptide selected from the group consisting of polylysine, polyglutamic acid, polyaspartic acid, a poly (Lys-Glu) co-polymer, a poly(Lys-Asp) copolymer, a poly(Lys-Ala-Glu-Tyr) (KAEY; 5:6:2:1) co-polymer or a polypeptides of from 2-50 residues chain length.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 3378587 A

L8: Entry 2 of 2 File: USOC Apr 16, 1968

DOCUMENT-IDENTIFIER: US 3378587 A
TITLE: 3, 3'-diaminomethyl-1, 1'-biadamantane

OCR Scanned Text (4):
7 ping off the toluene. The methaerylate polymerizes to colorless, crosslirked resins in the prese-ce of peroxides. Example 18.-3,3'-bis(p-phe@ioxypheiiyl)- 1,1'-b;adamantane A rrixture of 5 g. of 3,3'-dibromo-1,1'-biadama-iit@tne and 30 ml. of diphenyl ether is heated to 250' C. for four hotirs. The HBr formation ceases af'Ler about orie hour. The liquid reaction product is ,illowed to cool to room temperature and rpethaiiol is added to crystallize a white solid, - which is filtered jff a-@id- recryslallized froir acetone. T'--ie physical properties of the compound oblaiiied show the product to be 3,3' - bis(p - phenoxypheiiyl) - 1,1'biadamantane. Exa@mple 19.-3,3'-di-(p-hydroxyphenyl)- 1,1'-biadamanta,ic 5 g. of 3,3'-dibromo-1,1'-biadamantane and 30 @-. pher.ol are reacted by lieatin-, slowly uider a slow stream of i,itrogen (to rer,.iove HBr as formed) and sti.-rin.-. Hydrobrl- ir@ic acid formation b,-gins at 50' C. and at temperatures above 85' C. is rapid. After 36 minutes, the reiluxing temperature is 182' C. and the product is re'luxed ai i additional 30 r@ii,-iutes. On cooling to i-oom tem- perature, a white solid proci,,)itates and is refluxed @vith about 500 ml. of methanol. The solid remaining in the pot is filtered off in the hot state and washed wi'Lh ireth@ anol. Tlc y-'eld is 5.2 g., whicli is ne-arly quantitat;ve. The product is recrystallized for a@ialysis from dimetbyl acetamide ai-id tetrahydrofuran, givin- fiiie le,-,flets of melting point 343-344' C., solible iii hot dimethyl acetamide and tetrahydrofu,-an, insoluble in water, dioxane, w-etha@nol, benzene, CC'4, cyr-lohexane and 50% aqueous NAOH. C,-2H3802 (454.7), calc.: C, 84-53; H, 8.42. Four@d: C, 84.07; H, 8.54. There are also provided, accordin.a to this invention, a new class of pol@,mers havin- unusual properties. These polymers have E@.n iiiherent viscosify of at least 0.1 at 25' C. in a 1:1 mixture of 1,1,2-trichloroethane and phenol at a polymer concentration of 0.1% by weight, and are char-,icterized by repeating structural u-,iits, at least 50% of which contain an adamarityl or adamantylene radical. Pol@yi@-iers containin.- a predominant proportion of adamantyl or adamantylene groups exiiibit exceptional stability as well as very high melting points. These polymers are not only very stable toward beat-retaining good color over extended pcriods of time at high temperatures, but are also extraordinarily resistant to attack by acids, bases and ordinary solve-,its, making them very useful in applications calli-,- for hardness and dur,,ibility in contact @with corrosive materials. The film formiil- ability of the polymers and their stab-ilily and hardness renders them useftil as protective coatin-s. Polymers of tiis inver.,,ion may be prepared from any (-f the above described biadamantane or bisadam,,intyl compounds containing suitable polymerizable flnctional groups or which may be mcdified to contain stich groups. Ho@-nopoly.,-.iers may be produced or other copolymerizab!e n-ionopiers i,-E@,y be reacted with the above adan-anta,,,e derivatives to produ - ce copolymers provided that at least 50% of ttie structural units in such polymers contain an adaroantyl or adamantylene radical and at least 50% of the total wei,,,bt of the polymer is provided by siich radicals. Illustrative of the condensatioii polymers of this invention is the polyester formed by condensin,@ di-,i-icthylada@i-iantyl-1,3-dic-ai-boxylate witl-i 1,3-dimethylol adamanti,iie. The polyn7@er has the repeatir@g structural unit 0 F o lo@ ii L -C-A-C- OCIT@-A-CT121 - 31378) 587 forms a hard glossy film usclul ,is a protective coatii,,@. It is extrem-,Iy stable a-ainst attgck by ordi,-aary or.- aiiic solveiits and even concentrated hydrochlor@' c acicls, 90% forniic acid and 5 I@d sodium hyd,- ox;de at room tem- peratu re. It is soluble in a 50:50 mixture of phenol aiad 1,1,2- trichloroetha n--. Ti-,e polymer -ielts at about 250' C. and produces a colorless trarsparent film. Heatin.- the polymer for ei.-ht hours in an open test tub- . at 3251 C. produced no decoii@positi o.,i or even e- iscoloration. 10 Addi- i-on polyn-iers of this inve- @ition having the rercatiig structtir al unit RI R2] F I L Al-f where RI and R2 may be the same or differeqt and -nay be hydroge n, alkyl or any other radical Nvhich v,,hen a 2o substi'@ U-.nt on the r/- carbon atorn of acr3,lic acid does not prevent the polymeri zalion thereo'L tinder conventi onal polymeri zation condition s, and Al is a monoval. -nt radical corttaini ng an adamani yl grolp, preferab ly a carbada mantylo xy group. - D Prefer red among the addition rolymers of th;s invep--)@ tion is poly(ada mantyl riiethacr ylate). This po'- Ymer provides protec'Li ve coatipg s,,ibstar @tially superior ii some respccts to poly(met hyl@iiet hacrylat e) and poly(isob ornyl) rnethacr ylate. Ir@ additioi to exhibitin g hardness equivale- ,it 30 to fllms of the lalter two polymer s, poly(kad ama,.- @tyl x@.-thacrylat e) films provide cors:id,- rably higli i- @nprinti ng r- .sistance. The followi ng --

xamp' es illuslra te +he prepa ration of poiym ers of this i@iv.- ntion. @, 5 Example ZO.- Polyester from adamantane dicarboxylic acid dimet hyl ester- (1,3) and ethyle ne gl@yc o@L 13.6 g. of adam antan e d@ica rboxyl ic ac:d dimet hyl ester(1,3) (0.053 9 mole), 7.4 -. of ethyle re glycol (0.12 40 mole), 0.022 g. of calciul@ acetate dihydrate (0.15% based on diester), and 0.005 -. antimony dioxide (0.035% based on diester) are charge'd into a rolymer tlibe - ,Lqtted with a side arm (take off for methanol a-,id ethylene glycol) and an opening at the top for the introduction of 45 a capillary. The side arm of the i)olymer tube is connected to two cold traps @vhi,-h - @,vere - cooled w;th Dry Ice- acetone. TI-ie polymer tube is slowly heated to 75' C. in a silicone oil bath to obtain a melt. A,capiliary through the neck of the polymer tube reaches the bottom of the tube, 50 and nitrogen is slowly bubbled through the melt. The polymer tube is then heated to 157' C. whereby the distillat;on of methanol begins. The ternperatu re is then increased to 290' C. over a period of 4.5 hours and metbanol and excess .-lycol distill into the cold traps. Now 55 vacuum is applied and th-- condensati on is carried on for an additional three hours at 300' C. A viscous brownisii melt of poly(ethyle ne adamantyl dicarboxyl ate) solidifies on cooling. Example 21.- Polyamide from 3,3'-dicyano-1,1'-diadam- 60 antane and formaldehyde About 0.65 g. 3,3'- dicyan o-1,1'- diada manta ne, 10 ml. of conce ntrate d sulfuri c acid, and 7.5 ml. of formal dehyd e (37%) are charg ed irl- to an Erien meyer flgsk and stirred 65 for 15 minutes at room temperatur e. Then the reaction product is slowly heated to 75' C. aild a transparen t, sli.-htly yellow solution is obtained. The solution is stirred i-iito 100 ml. of ice water whereby a -,vhite t)roduct precipi- tates which is filtered off and washed wi@h water. About 70 0.75 -. of a white powder is obtained after dryin@ for three hours at 80' C. under vacuum. The product melts at around 230' C. and forms a highly viscous melt. The polymer is soltible in dimethyl acetam;de, insoluble in carbc)n teti-ach!oride, benzene and acetone. The infrared iii w'@licli A is aii ada-tiiantylene r@idical. 'f'l-.is polyiiier 7,5 spectrum is in agreement with the stated structure.

Term	Documents
POLY	338299
POLIES	67
POLYS	758
LYS-ASP	22
LYS-ASPS	0
K$1D	0
KAD	626
KBD	696
KCD	330
KD	41980
KDD	582
(POLY(LYS-ASP) OR POLY(K$1D)).PGPB,USPT,USOC.	2

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DATE: Monday, February 28, 2005

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☐	L10	PEG same RGD same $2polymer	22
☐	L9	PEG with RGD same $2polymer	9
☐	L8	poly(lactic acid with lysine) and RGD	4
	DB=; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L7	L6	1
	DB=PGPB,USPT,USOC; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L6	5399665.pn.	1
☐	L5	poly(lactic acid-co-lysine) and RGD	23
☐	L4	L3 and repetitive	2
☐	L3	RGD with copolymer	46
☐	L2	20040209818	1
☐	L1	5700906.pn.	1

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Search Results - Record(s) 1 through 22 of 22 returned.

☐ 1. Document ID: US 20050025821 A1

L10: Entry 1 of 22 File: PGPB Feb 3, 2005

DOCUMENT-IDENTIFIER: US 20050025821 A1
TITLE: Lipid-comprising drug delivery complexes and methods for their production

Detail Description Paragraph:
[0352] For the 10 mol % pegylated lipid formulations, 2191.5 nmol of DOPS or DOPG and 1394.59 nmol cholesterol and 398.45 nmol of 1,2-disteraoyl-sn-glycero-3-phosphotidylethanolamine-N-[methoxy(polyethyl- ene glycol)-5000](DSPE-PEG.sub.5K) (Shearwater Polymer Inc., Huntsville, Ala.) were prepared as described above. Typically, for 10 mol % targeting factor-pegylated lipid conjugate, targeted DLPD were prepared using 2191.5 nmol of DOPS or DOPG, 1394.59 nmol cholesterol and either 398.45 nmol DSPE-PEG.sub.5K-succinyl-ACDCRGDCFCG-COOH (DSPE-PEG.sub.5K-RGD) (SEQ ID NO: 10) or 398.45 nmol of pyrGLU-HWSY.sub.DK(.epsilon.NH-succinyl-PEG.- sub.5K-DSPE)LRPG-COOH (DSPE-PEG.sub.5K-LHRH) (SEQ ID NO:11). The conjugated lipids were synthesized by Integrated Biomolecule Corporation (Tucson, Ariz.). Briefly, for targeted liposomes, anionic lipid, cholesterol and DSPE-PEG.sub.5K-LHRH (SEQ ID NO:11) or DSPE-PEG.sub.5K-RGD (SEQ ID NO:10) were solubilized in chloroform at 20 mg/ml and were evaporated under nitrogen as described above. The lipid film was then re-solubilized in methanol:dichloromethane 1:1 (methanol from VWR, West Chester, Pa. and dichloromethane from EM science, Gibbstown, N.J.), re-evaporated under nitrogen prior to hydration in 0.15 ml 200 mM OGP, and subsequently processed as described above.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 20040213756 A1

L10: Entry 2 of 22 File: PGPB Oct 28, 2004

DOCUMENT-IDENTIFIER: US 20040213756 A1
TITLE: Methods and compositions to treat myocardial conditions

Detail Description Paragraph:
[0198] Example 1. Example 1 illustrates one possible three-component system described in FIG. 7 to treat a myocardial infarction. A cross-linking functionality can be synthesized starting from a fluorinated molecule with an ethylene functionality as in FIG. 22. Bromine 2310 is added to a fluoronated molecule 2300. Reduced thiols rapidly replace the bromine groups forming a di-functional thiol component 2320. The di-functional thiol 2330 can then react with a tetra-acryloyl(polyethylene glycol) 2340 and a difunctional polyethylene glycol with both the thiol functionality and the RGD 2380 peptide sequence. The tetra-acryloyl(polyethylene glycol) can be obtained from Shearwater Polymers as a specialty polymer (product number 0J0000D04; M.sub.r=2,000 with each arm having a molecular weight of 500 g/mol or .about.15 PEG sequences

long). It is generated by the reaction of the tetra-hydroxyl terminated polyethylene glycol and acryloyl in the presence of a tertiary amine.

☐ 3. Document ID: US 20040208845 A1

L10: Entry 3 of 22 File: PGPB Oct 21, 2004

DOCUMENT-IDENTIFIER: US 20040208845 A1
TITLE: Methods and compositions to treat myocardial conditions

Detail Description Paragraph:
[0201] Example 1 illustrates one possible three-component system described in FIG. 7 to treat a myocardial infarction. A cross-linking functionality can be synthesized starting from a fluorinated molecule with an ethylene functionality as in FIG. 22. Bromine 2310 is added to a fluoronated molecule 2300. Reduced thiols rapidly replace the bromine groups forming a di-functional thiol component 2320. The di-functional thiol 2330 can then react with a tetra-acryloyl(polyethylene glycol) 2340 and a difunctional polyethylene glycol with both the thiol functionality and the RGD 2380 peptide sequence. The tetra-acryloyl(polyethylene glycol) can be obtained from Shearwater Polymers as a specialty polymer (product number 0J0000D04; M.sub.r=2,000 with each arm having a molecular weight of 500 g/mol or .about.15 PEG sequences long). It is generated by the reaction of the tetra-hydroxyl terminated polyethylene glycol and acryloyl in the presence of a tertiary amine.

☐ 4. Document ID: US 20040127640 A1

L10: Entry 4 of 22 File: PGPB Jul 1, 2004

DOCUMENT-IDENTIFIER: US 20040127640 A1
TITLE: Composition, method and use of bi-functional biomaterials

Summary of Invention Paragraph:
[0010] Materials with surfaces that resist protein adsorption and fouling have also been developed. These materials may be further modified with biologic components to promote specific molecular and/or cellular interactions. Polymers such as poly(ethylene glycol) or PEG that resist protein binding are suitable to use for these modifications. In addition, peptides such as those containing RGD sequences (e.g., acrylamidoyl peptides) may be incorporated into mixtures of PEG diacrylate to create a peptide-modified polymer. Unfortunately, this technique is unable to control the spatial orientation of peptides on the material (i.e., polymer) surface and only works with biologic structures of limited type and size. This type of modification is limited to polymers that have the ability for Pegylation, which can be important for immobilization of peptide via covalent reactions.

☐ 5. Document ID: US 20040022842 A1

L10: Entry 5 of 22 File: PGPB Feb 5, 2004

DOCUMENT-IDENTIFIER: US 20040022842 A1
TITLE: Liposome preparations containing oxaliplatin

Summary of Invention Paragraph:
[0007] The present invention provides a formulation of liposomes containing oxaliplatin contained within the liposomes. The liposomes are derivatized with a hydrophilic polymer and a ligand. In various embodiments the ligand is selected from the group consisting of transferrin, folic acid, hyaluronic acid, a sugar chain such as galactose or mannose, a monoclonal antibody, pyridoxal phosphate, vitamin B12, sialyl Lewis X, epidermal growth factor, basic fibroblast growth factor, vascular endothelial growth factor, vascular cell adhesion molecule (VCAM-1), intercellular adhesion molecule (ICAM-1), platelet endothelial adhesion molecule (PECAM-1), an Arg-Gly-Asp (RGD) peptide, or an Asp-Gly-Arg (NGR) peptide, and a Fab' fragment of a monoclonal antibody. In various embodiments the hydrophilic polymer is selected from the group consisting of polyethylene glycol (PEG), polymethylethylene glycol, polyhydroxypropylene glycol, polypropylene glycol, polymethylpropylene glycol, and polyhydroxypropylene oxide. In one embodiment the hydrophilic polymer is polyethylene glycol and the ligand is transferrin.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

☐ 6. Document ID: US 20030220245 A1

L10: Entry 6 of 22 File: PGPB Nov 27, 2003

DOCUMENT-IDENTIFIER: US 20030220245 A1
TITLE: Conjugate addition reactions for the controlled delivery of pharmaceutical active compounds

Detail Description Paragraph:
[0166] One can incorporate peptide sites for cell adhesion, namely peptides that bind to adhesion-promoting receptors on the surfaces of cells into the biomaterials of the present invention. It is straightforward to incorporate a variety of such adhesion-promoting peptides, such as the RGD sequence from fibronectin or the YIGSR sequence from laminin. As above, this can be done, for example, simply by mixing a cysteine-containing peptide with PEG diacrylate or triacrylate, PEG diacrylamide or triacrylamide or PEG diquinone or triquinone a few minutes before mixing with the remainder of the thiol-containing precursor component. During this first step, the adhesion-promoting peptide will become incorporated into one end of the PEG multiply functionalized with a conjugated unsaturation; when the remaining multithiol is added to the system, a cross-linked network will form. Thus, for example, when an adhesion peptide containing one cysteine is mixed with a PEG triacrylate (at, e.g., 0.1 mole of peptide per mole of acrylate end group), and then a protease substrate peptide containing two cysteine residues is added to form the three-dimensional network (at, e.g., equimolar less 0.1 mole peptide per mole of acrylate end group), the resulting material will be highly biomimetic: the combination of incorporated adhesion sites and protease sites permits a cell to establish traction in the material as it degrades a pathway for its migration, exactly as the cell would naturally do in the extracellular matrix in vivo. In this case, the adhesion site is pendantly incorporated into the material. One could also incorporate the adhesion site directly in to the backbone of the material. This could be done in more than one way. One way would be to include two or more

thiols (e.g., cysteine) in the adhesion peptide or protein. One could alternatively synthesize the adhesion peptide (e.g., using solution phase chemistry) directly onto a polymer, such as PEG, and include at least one thiol (e.g., cysteine) or conjugated unsaturation per chain end.

Detail Description Paragraph:
[0529] A mixture (1 mL) of PEG-3400 diacrylamide and PEG-3400 .alpha.-monoacrylamide, .omega.-mono(paclitaxel side chain methyl ester) (Example 16) is incubated at 37.degree. C. for one hour. The peptide GCNNRGDNNCG (31.0 mg, 27.6 .mu.mol), which contains an RGD sequence for targeting to cells, can also be included in this mixture at a ratio of one thiol to one acrylamide. This method is expected to produce a linear high molecular weight copolymer of PEG-3400 and peptide which is end capped with PEG-3400 mono(paclitaxel side chain methyl ester) that can be formulated as an injectable composition.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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7. Document ID: US 20030185787 A1

L10: Entry 7 of 22 File: PGPB Oct 2, 2003

DOCUMENT-IDENTIFIER: US 20030185787 A1
TITLE: Methods and compositions to prevent formation of adhesions in biological tissues

Summary of Invention Paragraph:
[0032] Additional polymeric components, domains, linking groups, and bioactive, prophylactic, or diagnostic materials can be added to this basic two domain structure. Examples of additional polymeric components for attachment of linking groups, and bioactive, prophylactic, or diagnostic materials include PEG, polyacrylic acid, poly-N-vinyl pyrrolidone, hyaluronic acid, and other polysaccharides. Other domains that can be incorporated include bioadhesive molecules, domains which convert from a binding domain to a nonbinding domain in vivo, and domains which convert from a nonbinding domain to a binding domain in vivo, as described in U.S. Pat. No. 5,410,016 to Hubbell et al. Examples of linking groups include biodegradable linkages, such as anhydride, ester, amide, and carbonate linkages. Examples of bioactive materials include proteins, sugars and polysaccharides, organic compounds with drug activity, and nucleic acids. The domains and/or linkages can selectively adhere to particular types of cells or molecules or be selectively degraded by enzymatic or nonenzymatic means. The domains may be a third type of polymer, for example, a biodegradable polymer such as a polyanhydride, polyhydroxy acid or polycarbonate. A peptide such as RGD, or even a single amino acid, which is used to target a polyamino acid for cleavage by an enzyme, can be incorporated into the polymer structure, to direct attachment, as discussed in more detail below.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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8. Document ID: US 20030152548 A1

L10: Entry 8 of 22 File: PGPB Aug 14, 2003

DOCUMENT-IDENTIFIER: US 20030152548 A1
TITLE: Synthesis and characterization of biodegradable cationic poly (propylene fumarate-co-ethylene glycol) copolymer hydrogels modified with agmatine for enhanced cell adhesion

Detail Description Paragraph:
[0033] The incorporation of Agm-PEGF into P(PF-co-EG) hydrogels was shown qualitatively by staining the hydrogels with BPB. BPB has one sulfonyl group and is negatively charged at pH 6.8, the range at which the BPB staining was performed. Hydrogels without staining showed no absorbance at 590 nm. Experimental results suggest that the Agm-PEGF is incorporated into the hydrogel dose-dependently. Only a slight amount of the Agm-PEGF was detected. This result suggests that cross-linking is not sufficient for the incorporation of the feed Agm-PEGF into hydrogels, or that Agm-PEGF or the guanidino groups degrade during cross-linking. Since the NMR spectrum indicates that all ester bonds of Agm-PEGF were not hydrolyzed after the Agm-PEGF was dried from ddH.sub.2O by rotovaporation at 75.degree. C., it may not be possible that Agm-PEGF degraded during cross-linking. Shin et al. demonstrated the enhanced adhesion of marrow stromal osteoblasts to hydrogels modified with Arg-Gly-Asp (RGD) peptides fabricated through radical cross-linking by redox initiators of ascorbic acid and ammonium persulfate. The amount of the incorporated RGD peptide was not quantified. However, the peptide maintained its function after the cross-linking reaction. These results suggest that the cross-linking does not affect the chemical structure of guanidino group. Therefore, the reason for the insufficient incorporation may be due to the low cross-linking reactivity of Agm-PEGF. Most ionic hydrogels reported previously are vinyl-based hydrogels. The double bond of fumarate is thought to be less reactive than that of vinyl group because of the electroinductive effect of the carbonyl groups. In addition, P(PF-co-EG) is a block copolymer, and the cross-linkable fumarate unit exists in the hydrophobic portion of the copolymer. The cross-linkable fumarate of Agm-PEGF exists between PEG chains. Therefore, it is possible that the Agm-PEGF macromer's fumarate double bond may be sterically hindered the PPF portion of P(PF-co-EG) block copolymer. Another reason for the low Agm-PEGF content may be related to the reproducibility of the BPB staining method. Acid Orange 7 was used for quantification of positive charge contents in cationically modified surface and poly(acrylamide-dimethylaminoethyl methacrylate) hydrogels by analyzing the extracted dye. Staining conditions, such as pH and time, may affect the results. Absorbance of the adsorbed BPB was measured directly, but the adsorption of BPB to the hydrogels may affect the spectroscopic characteristics of BPB. Further optimization is required for a quantitative analysis by this method.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 9. Document ID: US 20030059906 A1

L10: Entry 9 of 22 File: PGPB Mar 27, 2003

DOCUMENT-IDENTIFIER: US 20030059906 A1
TITLE: Block copolymers for multifunctional self-assembled systems

Summary of Invention Paragraph:
[0033] By "adhesion peptides" is meant a peptide that binds to an adhesion-promoting receptor. It is straightforward to incorporate a variety of adhesion-promoting peptides that bind to adhesion-promoting receptors on the surfaces of cells, such as the RGD sequence from fibronectin or the YIGSR sequence from laminin. This can be done, for example, simply by mixing a cysteine-containing peptide with PEG diacrylate. During this step, the adhesion-promoting peptide becomes incorporated into one end of the PEG diacrylate; after purification of the product, the other end then reacts with a thiol-terminated polymer chain. In this case the adhesion site is pendantly incorporated into the material. One can also incorporate the adhesion site directly into the spine of the material. For example, one can synthesize the adhesion peptide (e.g., using solution phase chemistry) directly onto a polymer, such as PEG, and include at least one thiol (e.g., cysteine) per chain end and perform the same operation described above. Alternatively, one can include two or more thiols (e.g., cysteine) in the adhesion peptide or protein and let one react with PEG acrylate and the second initiate the

episulfides polymerization. Alternatively, one can attach an adhesion peptide to the surface of a preformed self-assembled aggregate, such as the surface of a preformed micelle or vesicle. For example, the copolymer can be end-capped with a Michael acceptor, such as those groups described above. This end-capping can be readily accomplished by reacting the thiol-containing AB block copolymer with an excess of a PEG diacrylate to yield an ABA' copolymer that is terminally functionalized with an acrylate group. Micelles or vesicles can be formed from this material. A peptide containing a free cysteine can be dissolved in a suspension of these micelles or vesicles and the pH adjusted to a range where a Michael-type addition between the self-assembled aggregate-bound acrylate reacts with the free thiol on the adhesion peptide.

☐ 10. Document ID: US 20030012816 A1

L10: Entry 10 of 22 File: PGPB Jan 16, 2003

DOCUMENT-IDENTIFIER: US 20030012816 A1
TITLE: Nitric oxide-producing hydrogel materials

Detail Description Paragraph:
[0131] In order for these hydrogels to effectively prevent restenosis, re-endothelialization must occur not only in areas surrounding the hydrogel, but also upon the hydrogel itself. To investigate the proliferation of endothelial cells cultured on NO-releasing hydrogels, a cell adhesion ligand was first covalently incorporated into these hydrogels, as cells will not attach to PEG unless the polymer is modified with an adhesive sequence (Hem D, Hubbell J. Incorporation of adhesion peptides into nonadhesive hydrogels useful for tissue resurfacing, J Biomed Mater Res 1998; 39: 266-276). To achieve this, hydrogels containing the adhesive peptide sequence RGDS (Arginine-Glycine-Aspartic acid-Serine) and the NO donor DETA-NO were synthesized. RGDS was covalently bound to PEG by reaction with ACRL-PEG-NHS in a ratio of 1:2 (RGDS:polymer) in 50 mM sodium bicarbonate buffer (pH 8.5) for two hours at room temperature. The solution was then dialyzed and lyophilized to obtain ACRL-PEG-RGDS. ACRL-PEG-DETA-NO was prepared as described above. These two copolymers were blended with PEG-diacrylate to achieve a final RGDS concentration of 1.4 .mu.mol/ml of polymer, and 1.25 .mu.mol DETA-NO/ml of polymer, which would theoretically deliver a total of 50 nmol NO donor per ml of cell culture media. The hydrogel precursor solution was filter sterilized and poured between two polystyrene plates separated by a 400 .mu.m gap. The hydrogel precursor was exposed to UV light, and a sterilized cork-borer punch (Cole Parmer, Vernon Hills, Ill.) was used to create thin, circular hydrogels that were subsequently placed in a 24-well plate. BAECs were immediately seeded upon the hydrogels at a density of 7500 cells/cm.sup.2. Controls consisted of hydrogels with the NO donor alone or RGDS alone. Two days after cell seeding, cells were trypsinized and cell number was assessed by counting on a Coulter Counter.

☐ 11. Document ID: US 20020106793 A1

L10: Entry 11 of 22 File: PGPB Aug 8, 2002

DOCUMENT-IDENTIFIER: US 20020106793 A1
TITLE: Tissue engineering scaffolds promoting matrix protein production

Detail Description Paragraph:
[0059] Hydrogels were prepared by combining 0.4 g/ml PEG-diacrylate, 1.4 .mu.mol/ml acryloyl-PEG-RGDS (SEQ ID NO:1), and 0.3 mmol/ml triethanolamine in 10 mM HEPES-buffered saline (pH 7.4, HBS). This aqueous polymer solution was sterilized by filtration (0.8 .mu.m prefilter and 0.2 .mu.m filter) and added to an equal volume of a suspension of SMCs at 2.times.10.sup.6 cells/ml, such that the resulting polymer-cell solution contained 1.times.10.sup.6 cells/ml. For hydrogels containing TGF-.beta., 0.04 pmol/ml (1 ng/ml) unmodified TGF-.beta. or 0.04 pmol/ml acryloyl-PEG-TGF-.beta. was added to the polymer-cell solution. Then, 40 .mu.l of 2,2-dimethyl-2-phenyl-acetophenone in n-vinylpyrrolidone (600 mg/ml) was added, and 0.25 ml of the solution was placed in a disk-shaped mold (20 mm diameter, 2 mm thickness). This liquid polymer-cell solution was then exposed to UV light (365 nm, 10 mW/cm.sup.2) for 20 sec to convert the liquid polymer-cell solution to a hydrogel with homogeneously seeded cells. Hydrogels were incubated in MEM containing 10% FBS for 7 days at 37.degree. C. with 5% CO.sub.2. Media was changed every 3 days.

Detail Description Paragraph:
[0070] Cells seeded onto RGDS (SEQ ID NO:1)-modified glass surfaces were also grown in the presence of 0.04 pmol/ml acryloyl-PEG-TGF-.beta. to determine if TGF-.beta. could be covalently bound to a polymer (covalently attached to a soluble polymer chain but not tethered to a three dimensional structure) and retain its ability to increase ECM production. FIG. 2 shows the matrix production by cells grown with no TGF-.beta., soluble TGF-.beta., or acryloyl-PEG-TGF-.beta. in the media. SMCs produced greater amounts of matrix in the presence of either soluble or polymer-conjugated TGF-.beta. over that produced in the absence of TGF-.beta.. However, less matrix was produced when polymer-conjugated TGF-.beta. was used than when unmodified TGF-.beta. was used.

☐ 12. Document ID: US 20010047081 A1

L10: Entry 12 of 22 File: PGPB Nov 29, 2001

DOCUMENT-IDENTIFIER: US 20010047081 A1
TITLE: Adenoviral capsid containing chimeric protein IX

Detail Description Paragraph:
[0019] However produced, the chimeric pIX protein can be incorporated into an adenoviral capsid. Thus, the invention provides an adenoviral capsid containing a chimeric pIX protein as described above. In addition to the chimeric pIX protein, the capsid can be further modified, for example, through the inclusion of other recombinant proteins. For example, the capsid can have one or more mutant adenoviral fiber proteins exhibiting reduced affinity for a native adenoviral cellular receptor (typically at least about an order of magnitude less than a wild-type adenoviral fiber protein) (see, e.g., International Patent Application WO 98/54346 (Wickham et al.)). Moreover, the capsid can include one or more recombinant penton base proteins lacking a native RGD sequence to reduce cell binding via a, integrins (see, e.g., U.S. Pat. Nos. 5,559,099 (Wickham et al.) and 5,731,190 (Wickham et al.)). Similarly, the capsid can include one or more recombinant hexons lacking native sequences (e.g., one or more of the hypervariable regions (HVRs) to reduce its ability to be recognized by a neutralizing antibody (see, e.g., International Patent Application WO 98/40509 (Crystal et al.)). Also, the capsid can be modified to reduce its ability to interact with the reticular endothelial system, thereby decreasing its ability to be scavenged by the immune system. For example, capsid proteins can be mutated to lack one or more glycosylation or phosphorylation sites, or capsid proteins can be produced in the presence of inhibitors of glycosylation or phosphorylation.

Similarly, the virion proteins can be conjugated to polyethylene glycol to reduce collectin and/or opsonin affinity or scavenging by Kupffer cells or other cells of the RES. Such modifications reduce the ability of host animals to develop neutralizing antibodies to the capsid, thereby permitting repeat administration (see, e.g., O'Riordan et al., Hum. Gene Ther., 19(8):1349-1358 (1999); Chillon et al., Gene Ther., 5(7): 995-1002 (1998)). Of course, the hydrophilic polymer PEG is only a preferred polymer and any molecule that sterically blocks recognition of the virion proteins by the host immune system, thus masking the adenoviral vector surface by covalent attachment of the molecule, can be used in the context of the present invention.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 13. Document ID: US 20010027237 A1

L10: Entry 13 of 22 File: PGPB Oct 4, 2001

DOCUMENT-IDENTIFIER: US 20010027237 A1
TITLE: Comb copolymers for regulating cell-surface interactions

Detail Description Paragraph:
[0097] Mixtures of polylactide, PLA, homopolymer and small amounts of the non-cell binding or RGD-bearing comb copolymers (10 wt % or less relative to PLA) were dissolved in toluene, and cast as films on glass. Films were subsequently dried under vacuum for 24 hours to remove residual solvent. Some of the comb/PLA films were subsequently annealed 96 hours in a 70.degree. C. water bath. X-ray photoelectron spectroscopy studies showed significant enrichments of the comb copolymer at the surface of annealed blends (.about.60% by volume comb copolymer at the surface for a 10% bulk concentration). Advancing/receding contact angle measurements similarly indicate that the annealed blend films have substantially lower water contact angles than PLA and exhibit a large hysteresis indicative of PEG side chain reorientation/hydration at the surface when in contact with water.

Detail Description Paragraph:
[0110] To obtain adhesion ligand-bearing non-biodegradable combs, the RGD peptide was attached to hydroxyl end groups of the PEG side chains. The combs were dissolved in anhydrous tetrahydrofuran (THF), followed by addition of triethylamine and tresyl chloride, and reacted for 90 minutes. The activated polymer was recovered by precipitation in anhydrous methanol, and stored at -70.degree. C. until use. RGD was coupled through primary amines to the activated combs by first dissolving the combs in dry THF, followed by addition of peptide solution (1 mg/mL GRGDSP in phosphate buffered saline (PBS)) at a ratio of 10:1 THF:PBS. Coupling was allowed to proceed with stirring for 3 hours at 5.degree. C. The resulting RGD-comb polymer was recovered by precipitation/washing with deionized water.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 14. Document ID: US 6800296 B1

L10: Entry 14 of 22 File: USPT Oct 5, 2004

DOCUMENT-IDENTIFIER: US 6800296 B1
TITLE: Modification of surfaces using biological recognition events

Detailed Description Text (37):
Attachment and spreading of bovine aortic endothelial cells was observed on the PLA-PEG-biotin-avidin-biotin-(G)11-GRGDS (SEQ ID NO: 3) polymer surface at all time points, while no spreading was observed on negative controls which included samples composed of PLA-PEG, PLA-PEG-biotin, PLA-PEG-biotin-avidin, and PLA-PEG-biotin-avidin-biotin. In addition, no cell spreading was observed on samples of PLA-PEG-biotin which were incubated in biotin-(G)11-GRGDS (SEQ ID NO: 3), demonstrating the lack of nonspecific binding of the biotinylated RGD sequence to the polymer surface. The eleven glycine residue was provided to ensure clearance of the cell adhesive RGD sequence from the avidin binding pocket (Pierschbacher and Ruoslahti, Proc. Natl. Acad. Sci., U.S.A.,1984, 81, 5985; Green, "Avidin and Streptavidin" in Methods in Enzymology: Avidin-Biotin Technology, Vol 184, Academic Press, Inc., New York, 1990; Beer et al., Blood, 1992, 79, 117). FIG. 5 shows images of cells on the PLA-PEG-biotin and PLA-PEG-biotin-avidin-biotin-(G)11-GRGDS (SEQ ID NO: 3) surfaces along with a histogram of measured cell area for each sample.

☐ 15. Document ID: US 6740525 B2

L10: Entry 15 of 22 File: USPT May 25, 2004

DOCUMENT-IDENTIFIER: US 6740525 B2
TITLE: Adenoviral capsid containing chimeric protein IX

Detailed Description Text (14):
However produced, the chimeric pIX protein can be incorporated into an adenoviral capsid. Thus, the invention provides an adenoviral capsid containing a chimeric pIX protein as described above. In addition to the chimeric pIX protein, the capsid can be further modified, for example, through the inclusion of other recombinant proteins. For example, the capsid can have one or more mutant adenoviral fiber proteins exhibiting reduced affinity for a native adenoviral cellular receptor (typically at least about an order of magnitude less than a wild-type adenoviral fiber protein) (see, e.g., International Patent Application WO 98/54346 (Wickham et al.)). Moreover, the capsid can include one or more recombinant penton base proteins lacking a native RGD sequence to reduce cell binding via a, integrins (see, e.g., U.S. Pat. Nos. 5,559,099 (Wickham et al.) and 5,731,190 (Wickham et al.)). Similarly, the capsid can include one or more recombinant hexons lacking native sequences (e.g., one or more of the hypervariable regions (HVRs) to reduce its ability to be recognized by a neutralizing antibody (see, e.g., International Patent Application WO 98/40509 (Crystal et al.)). Also, the capsid can be modified to reduce its ability to interact with the reticular endothelial system, thereby decreasing its ability to be scavenged by the immune system. For example, capsid proteins can be mutated to lack one or more glycosylation or phosphorylation sites, or capsid proteins can be produced in the presence of inhibitors of glycosylation or phosphorylation. Similarly, the virion proteins can be conjugated to polyethylene glycol to reduce collection and/or opsonin affinity or scavenging by Kupffer cells or other cells of the RES. Such modifications reduce the ability of host animals to develop neutralizing antibodies to the capsid, thereby permitting repeat administration (see, e.g., O'Riordan et al., Hum. Gene Ther., 19(8):1349-1358 (1999); Chillon et al., Gene Ther., 5(7): 995-1002 (1998)). Of course, the hydrophilic polymer PEG is only a preferred polymer and any molecule that sterically blocks recognition of the virion proteins by the host immune system, thus masking the adenoviral vector surface by covalent attachment of the molecule, can be used in the context of the present invention.

☐ 16. Document ID: US 6596267 B1

L10: Entry 16 of 22 File: USPT Jul 22, 2003

DOCUMENT-IDENTIFIER: US 6596267 B1
TITLE: Methods and compositions to prevent formation of adhesions in biological tissues

Brief Summary Text (34):
Additional polymeric components, domains, linking groups, and bioactive, prophylactic, or diagnostic materials can be added to this basic two domain structure. Examples of additional polymeric components for attachment of linking groups, and bioactive, prophylactic, or diagnostic materials include PEG, polyacrylic acid, poly-N-vinyl pyrrolidone, hyaluronic acid, and other polysaccharides. Other domains that can be incorporated include bioadhesive molecules, domains which convert from a binding domain to a nonbinding domain in vivo, and domains which convert from a nonbinding domain to a binding domain in vivo, as described in U.S. Pat. No. 5,410,016 to Hubbell et al. Examples of linking groups include biodegradable linkages, such as anhydride, ester, amide, and carbonate linkages. Examples of bioactive materials include proteins, sugars and polysaccharides, organic compounds with drug activity, and nucleic acids. The domains and/or linkages can selectively adhere to particular types of cells or molecules or be selectively degraded by enzymatic or nonenzymatic means. The domains may be a third type of polymer, for example, a biodegradable polymer such as a polyanhydride, polyhydroxy acid or polycarbonate. A peptide such as RGD, or even a single amino acid, which is used to target a polyamino acid for cleavage by an enzyme, can be incorporated into the polymer structure, to direct attachment, as discussed in more detail below.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 17. Document ID: US 6468657 B1

L10: Entry 17 of 22 File: USPT Oct 22, 2002

DOCUMENT-IDENTIFIER: US 6468657 B1
TITLE: Controllable ion-exchange membranes

Detailed Description Text (98):
In a further preferred embodiment, R.sup.1 is a poly(ethyleneglycol) moiety. Polyethylene glycol (PEG) use in biotechnology and biomedical applications continuing to expand and has been reviewed (Poly(ethylene glycol) Chemisrty: Biotechnical and Biomedical Applications, J. M. Harris, Ed., Plenum Press, New York, 1992). Modification of enzymes (Chiu et al., J. Bioconjugate Chem., 4: 290-295 (1993)), RGD peptides (Braatz et al., Bioconjugate Chem., 4: 262-267 (1993)), liposomes (Zalipsky, S. Bioconjugate Chem., 4: 296-299 (1993)), and CD4-IgG glycoprotein (Chamow et al., Bioconjugate Chem., 4: 133-140 (1993)) are some of the recent advances in the use of polyethylene glycol. The modification of toxicity, pharmacokinetics, biodistribution and other biofunctions are a number of the promising areas for the use of this simple polymer. Surfaces treated with PEG have been shown to resist protein deposition and have improved resistance to thrombogenicity when coated on blood contacting biomaterials (Merrill, "Poly(ethylene oxide) and Blood Contact: A Chronicle of One Laboratory," in Poly(ethylene glycol) Chemistry: Biotechnical and Biomedical Applications, Harris, Ed., Plenum Press, New

York, (1992), pp. 199-220). Accordingly, application of PEG based coatings to multilayered porous materials would be very useful for chromatography, analytical and medical devices. In the present invention, hydrophilic polymers such as PEG can be used to engineer preselected pore sizes and characteristics by the judicious choice of the size of the PEG(s) chosen as constituents of the organic layer.

☐ 18. Document ID: US 6399700 B2

L10: Entry 18 of 22 File: USPT Jun 4, 2002

DOCUMENT-IDENTIFIER: US 6399700 B2
TITLE: Comb copolymers for regulating cell-surface interactions

Detailed Description Text (10):
Mixtures of polylactide, PLA, homopolymer and small amounts of the non-cell binding or RGD-bearing comb copolymers (10 wt % or less relative to PLA) were dissolved in toluene, and cast as films on glass. Films were subsequently dried under vacuum for 24 hours to remove residual solvent. Some of the comb/PLA films were subsequently annealed 96 hours in a 70.degree. C. water bath. X-ray photoelectron spectroscopy studies showed significant enrichments of the comb copolymer at the surface of annealed blends (.about.60% by volume comb copolymer at the surface for a 10% bulk concentration). Advancing/receding contact angle measurements similarly indicate that the annealed blend films have substantially lower water contact angles than PLA and exhibit a large hysteresis indicative of PEG side chain reorientation/hydration at the surface when in contact with water.

Detailed Description Text (27):
To obtain adhesion ligand-bearing non-biodegradable combs, the RGD peptide was attached to hydroxyl end groups of the PEG side chains. The combs were dissolved in anhydrous tetrahydrofuran (THF), followed by addition of triethylamine and tresyl chloride, and reacted for 90 minutes. The activated polymer was recovered by precipitation in anhydrous methanol, and stored at -70.degree. C. until use. RGD was coupled through primary amines to the activated combs by first dissolving the combs in dry THF, followed by addition of peptide solution (1 mg/mL GRGDSP in phosphate buffered saline (PBS)) at a ratio of 10:1 THF:PBS. Coupling was allowed to proceed with stirring for 3 hours at 5.degree. C. The resulting RGD-comb polymer was recovered by precipitation/washing with deionized water.

☐ 19. Document ID: US 6277489 B1

L10: Entry 19 of 22 File: USPT Aug 21, 2001

DOCUMENT-IDENTIFIER: US 6277489 B1
TITLE: Support for high performance affinity chromatography and other uses

Detailed Description Text (86):
In a further preferred embodiment, R.sup.1 is a poly(ethyleneglycol) moiety. Polyethylene

glycol (PEG) use in biotechnology and biomedical applications continues to expand and has been reviewed (POLY(ETHYLENE GLYCOL) CHEMISTRY. BIOTECHNICAL AND BIOMEDICAL APPLICATIONS, J. M. Harris, Ed., Plenum Press, New York, 1992). Modification of enzymes (Chiu el al., J. Bioconjugate Chem., 4: 290-295 (1993)), RGD peptides (Braatz et al., Bioconjugate Chem., 4: 262-267 (1993)), liposomes (Zalipsky, S. Bioconjugate Chem., 4: 296-299 (1993)), and CD4-IgG glycoprotein (Chamow et al., Bioconjugate Chem., 4: 133-140 (1993)) are some of the recent advances in the use of polyethylene glycol. The modification of toxicity, pharmacokinetics, biodistribution and other biofunctions are a number of the promising areas for the use of this simple polymer. Surfaces treated with PEG have been shown to resist protein deposition and have improved resistance to thrombogenicity when coated on blood contacting biomaterials (Merrill, "Poly(ethylene oxide) and Blood Contact: A Chronicle of One Laboratory," in POLY(ETHYLENE GLYCOL) CHEMISTRY: BIOTECHNICAL AND BIOMEDICAL APPLICATIONS, Harris, Ed., Plenum Press, New York, (1992), pp. 199-220). Accordingly, application of PEG based coatings to multilayered particulate materials would be very useful for chromatography, analytical and medical devices.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 20. Document ID: US 6207749 B1

L10: Entry 20 of 22 File: USPT Mar 27, 2001

DOCUMENT-IDENTIFIER: US 6207749 B1
TITLE: Comb copolymers for regulating cell-surface interactions

Detailed Description Text (10):
Mixtures of polylactide, PLA, homopolymer and small amounts of the non-cell binding or RGD-bearing comb copolymers (10 wt % or less relative to PLA) were dissolved in toluene, and cast as films on glass. Films were subsequently dried under vacuum for 24 hours to remove residual solvent. Some of the comb/PLA films were subsequently annealed 96 hours in a 70.degree. C. water bath. X-ray photoelectron spectroscopy studies showed significant enrichments of the comb copolymer at the surface of annealed blends (.about.60% by volume comb copolymer at the surface for a 10% bulk concentration). Advancing/receding contact angle measurements similarly indicate that the annealed blend films have substantially lower water contact angles than PLA and exhibit a large hysteresis indicative of PEG side chain reorientation/hydration at the surface when in contact with water.

Detailed Description Text (26):
To obtain adhesion ligand-bearing non-biodegradable combs, the RGD peptide was attached to hydroxyl end groups of the PEG side chains. The combs were dissolved in anhydrous tetrahydrofuran (THF), followed by addition of triethylamine and tresyl chloride, and reacted for 90 minutes. The activated polymer was recovered by precipitation in anhydrous methanol, and stored at -70.degree. C. until use. RGD was coupled through primary amines to the activated combs by first dissolving the combs in dry THF, followed by addition of peptide solution (1 mg/mL GRGDSP in phosphate buffered saline (PBS)) at a ratio of 10:1 THF:PBS. Coupling was allowed to proceed with stirring for 3 hours at 5.degree. C. The resulting RGD-comb polymer was recovered by precipitation/washing with deionized water.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 21. Document ID: US 6150459 A

L10: Entry 21 of 22 File: USPT Nov 21, 2000

DOCUMENT-IDENTIFIER: US 6150459 A
TITLE: Comb polymers for regulating cell surface interactions

Detailed Description Text (10):
Mixtures of polylactide, PLA, homopolymer and small amounts of the non-cell binding or RGD-bearing comb copolymers (10 wt % or less relative to PLA) were dissolved in toluene, and cast as films on glass. Films were subsequently dried under vacuum for 24 hours to remove residual solvent. Some of the comb/PLA films were subsequently annealed 96 hours in a 70.degree. C. water bath. X-ray photoelectron spectroscopy studies showed significant enrichments of the comb copolymer at the surface of annealed blends (.about.60% by volume comb copolymer at the surface for a 10% bulk concentration). Advancing/receding contact angle measurements similarly indicate that the annealed blend films have substantially lower water contact angles than PLA and exhibit a large hysteresis indicative of PEG side chain reorientation/hydration at the surface when in contact with water.

Detailed Description Text (26):
To obtain adhesion ligand-bearing non-biodegradable combs, the RGD peptide was attached to hydroxyl end groups of the PEG side chains. The combs were dissolved in anhydrous tetrahydrofuran (THF), followed by addition of triethylamine and tresyl chloride, and reacted for 90 minutes. The activated polymer was recovered by precipitation in anhydrous methanol, and stored at -70.degree. C. until use. RGD was coupled through primary amines to the activated combs by first dissolving the combs in dry THF, followed by addition of peptide solution (1 mg/mL GRGDSP in phosphate buffered saline (PBS)) at a ratio of 10:1 THF:PBS. Coupling was allowed to proceed with stirring for 3 hours at 5.degree. C. The resulting RGD-comb polymer was recovered by precipitation/washing with deionized water.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 22. Document ID: US 5650234 A

L10: Entry 22 of 22 File: USPT Jul 22, 1997

DOCUMENT-IDENTIFIER: US 5650234 A
TITLE: Electrophilic polyethylene oxides for the modification of polysaccharides, polypeptides (proteins) and surfaces

Brief Summary Text (6):
Polyethylene glycol (PEG) use in biotechnology and biomedical applications continues to expand and has recently been reviewed (1). Modification of enzymes (2), RGD peptides (3), liposomes (4), and CD4-IgG glycoprotein (5) are some of the recent advances in the use of polyethylene glycol. The modification of toxicity, pharmacokinetics, biodistribution and other biofunctions are a number of the promising areas for the use of this simple polymer. Surfaces treated with PEG have been shown to resist protein deposition and have improved resistance to thrombogenicity when coated on blood contacting biomaterials (6). Accordingly, application of PEG based coatings to various polymeric materials especially with respect to "continuous" coating of microporous hollow fiber or other plastic parts would be very useful for medical devices.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Term	Documents
PEG	71975
PEGS	24637
RGD	9038
RGDS	1486
$2POLYMER	0
POLYMER	531501
APOLYMER	153
CAPOLYMER	74
NAPOLYMER	3
OAPOLYMER	1
RAPOLYMER	3
(PEG SAME RGD SAME $2POLYMER).PGPB,USPT,USOC.	22

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